

IN THE CLAIMS

1. (currently amended): A method of separating a target oligonucleotide from an impurity, in a mixture comprising said target oligonucleotide and said impurity, using a titratable anion exchange composition, comprising the steps:
 - a) binding said target oligonucleotide to said titratable anion exchange composition at in the presence of a solution having a first pH; and
 - b) passing [a] solution through said titratable anion exchange composition with target oligonucleotide bound thereon, wherein the pH of said elution solution is increased over time to a pH higher than said first pH thereby to elute said target oligonucleotide, wherein said impurity elutes at a different pH than said target oligonucleotide, and wherein either
 - c) the elution solution is substantially free from metal salts such that subsequent desalting of the eluted oligonucleotide is not required; or
 - d) the elution solution does not substantially increase its salt concentration over time such that subsequent desalting of the eluted oligonucleotide is not required.
2. (original): The method of claim 1 wherein said titratable anion exchange composition comprises a primary amine, a secondary amine or a tertiary amine.
3. (original): The method of claim 1 or claim 2, wherein said titratable anion exchange composition comprises polyethylenimine, polyimidazole, polyhistidine or polylysine.
4. (previously presented): The method of claim 1, wherein said solution in b) is substantially free of metal salts such that subsequent desalting of the eluted target oligonucleotide is not required.
5. (previously presented): The method according to claim 1, wherein the solution in b) does not substantially increase its salt concentration over time such that subsequent desalting of the eluted target oligonucleotide is not required.
6. (previously presented): The method of claim 1, wherein said titratable anion exchange composition is conjugated to a support.
7. (original): The method of claim 6, wherein said support is a synthetic polymer.

8. (original): The method of claim 7, wherein said synthetic polymer is selected from the group consisting of silica gel, a polysaccharide, a styrene-divinyl benzene copolymer, a polyethylene, a polypropylene, a polyacrylic and an agarose.

9. (previously presented): The method of claim 8, wherein said titratable anion exchange composition is polyethyleneimine-derivatized silica gel or a polyethyleneimine-derivatized styrene-divinyl benzene copolymer.

10. (previously presented): The method of claim 1, wherein said target oligonucleotide is a synthetic oligonucleotide.

11. (previously presented): The method of claim 10, wherein said synthetic oligonucleotide is selected from the group consisting of a phosphorothioate, a phosphorodithioate, a methyl phosphonate and a phosphoramidate.

12. (previously presented): The method of claim 1, wherein binding of said target oligonucleotide with said titratable anion exchange composition occurs at a pH between 5 and 8.

13. (previously presented): The method of claim 1, wherein said solution in b) increases in pH in a linear manner over time.

14. (previously presented): The method of claim 1, wherein said solution in b) increases from a pH of about 8 to a pH of about 11.

15. (previously presented): The method of claim 1, wherein said solution in b) comprises one or more of NH_4HCO_3 and/or NH_4OH .

16. (previously presented): The method of claim 1, wherein said target oligonucleotide has a length from about 8 to about 40 nucleotides.

17. (previously presented): The method of claim 1, wherein said impurity is one or more oligonucleotides having a shorter length than said target oligonucleotide, and wherein said impurity elutes at a lower pH than said target oligonucleotide.

18. (original): The method of claim 17, wherein said impurity is one or more failure sequences.

19. (previously presented): The method of claim 1, wherein said impurity is a metal salt.
20. (previously presented): The method of claim 1, wherein said target oligonucleotide is 5'-O-protected.
21. (previously presented): The method of claim 20, wherein said target oligonucleotide is 5'-O-trityl protected.
22. (original): The method of claim 21, further comprising a step of passing through said titratable anion exchange composition a sufficient amount of an acidic solution to cleave said 5'-O-trityl protecting group from said target oligonucleotide prior to eluting said target oligonucleotide.
23. (original): The method of claim 22 wherein said acidic solution comprises aqueous acetic acid.
24. (previously presented): The method of claim 1, wherein said solution in b) has a volume which is less than the volume of the mixture comprising said target oligonucleotide and impurity, thereby increasing the concentration of said target oligonucleotide.
25. (previously presented): The method of claim 1, further comprising one or more washing steps prior to eluting said target oligonucleotide.
26. (previously presented): The method of claim 21, wherein said target oligonucleotide is 5'-O-dimethoxy-trityl protected.
27. (previously presented): The method of claim 1, wherein said titratable anion exchange composition comprises polyethyleneimine, polyimidazole, polyhistidine or polylysine conjugated to a synthetic polymer support; said solution in b) is substantially free of metal salts and does not substantially increase its salt concentration over time whereby subsequent desalting of the eluted target oligonucleotide is not required and said solution increases from a pH of about 8 to a pH of about 11 and comprises one or more of NH_4HCO_3 and/or NH_4OH .

28. (currently amended): A method of separating a target oligonucleotide from an impurity, in a mixture comprising said target oligonucleotide and said impurity, using a titratable anion exchange composition, comprising the steps:

- a) binding said mixture of target oligonucleotide and impurity to said titratable anion exchange composition at a first pH; and
- b) passing [a] an elution solution through said titratable anion exchange composition with the mixture of target oligonucleotide and impurity bound thereon, wherein the pH of said solution is increased over time to a pH higher than said first pH thereby to elute said target oligonucleotide, and wherein said impurity elutes at a different pH than said target oligonucleotide, and wherein either
- c) the elution solution is substantially free from metal salts such that subsequent desalting of the eluted oligonucleotide is not required; or
- d) the elution solution does not substantially increase its salt concentration over time such that subsequent desalting of the eluted oligonucleotide is not required.